

Lanthanide Ion Nuclear Magnetic Resonance Probe Studies of Benzoic Acids. The Agreement with an Axially Symmetric Model

B. T. PENNINGTON* AND J. R. CAVANAUGH†

Eastern Regional Research Center, Agricultural Research Service, USDA, Philadelphia, Pennsylvania 19118

The lanthanide-induced shift ratios measured in the presence of various lanthanide (3+) ions and the spin-lattice relaxation rates induced by Gd^{3+} were determined for benzoate, *o*-toluate, and *p*-toluate at pH 6.0. The data indicate that the shifts originate primarily from a pseudocontact mechanism with axial or near-axial symmetry. The shift ratios for given sets of protons were found to be consistent with this interpretation but suggest that the binding of the lighter Ln^{3+} ions differ slightly from that of the heavier members of the series. The best agreement between observed and predicted shift ratios for the lighter ions that could be obtained with a bidentate, axially symmetric model was one in which the principal symmetry axis lies in the plane of the carboxylate group and bisects the O—C—O bond angle. The proton T_1 ratios for Gd^{3+} complexes of *o*-toluate and *p*-toluate are consistent with the appropriate distance relationships with one exception. The relaxation time for the ortho proton relative to the ortho methyl proton of *o*-toluate is shorter than expected and suggests that either the Gd^{3+} ion is preferentially binding to the carboxylate oxygen nearer the ortho proton or the internal rotation of the methyl group is affecting the correlation time for the ortho methyl proton.

INTRODUCTION

Over the past few years, lanthanide ions have found increasing use as NMR structural probes of biologically important molecules (1–9). Lanthanide-induced shifts and relaxation data of carboxylate ligands have been fit to an axially symmetric model in which the principal magnetic axis bisects the carboxylate group (3). Often the approach has been to assume the presence of only one rotamer or conformer and to solve for the single conformation which agrees best with the lanthanide shift and relaxation data. However, the ligands in the carboxylate systems studied so far have all had some degree of flexibility, and certain compounds studied have had the possibility of multiple internal rotation (3, 4). Only if the conformer populations are known independently can the agreement between the measured and calculated parameters be determined with much certainty.

To facilitate the determination of the fit of various models, we investigated a system with known rigid structures, namely, *o*-toluic, *p*-toluic, and benzoic acids. The study of these ligands gave results which can be interpreted in a straightforward manner and provide useful information for future studies.

* NRC-ARS Postdoctoral Research Associate. Present address: Chemistry Department, Navarro College, Corsicana, Tex. 75151.

† Author to whom inquiries should be addressed.

EXPERIMENTAL

The hydrated chlorides of the tripositive metals Ce, Pr, Ho, Eu, Nd, Dy, Er, Gd, Yb (99.9%), and La (>99.9%) were obtained from Ventron, Alfa Products¹ and used without further purification. Benzoic acid (Baker analyzed) and the toluic acids (98%, Aldrich Chemical Company) were converted into their respective sodium salts which were purified by repeated recrystallization from water–acetone and oven drying at 50°C for 5 hr. Samples were prepared in aqueous dimethyl sulfoxide (DMSO) solutions to prevent precipitation of Ln^{3+} benzoates. The maximum concentration of DMSO used was 30% by volume. Carboxylate ligands are known to form higher than 1:1 complexes with the lanthanide ions in aqueous solution (10, 11). Therefore, we have kept the ratio of Ln^{3+} to ligand concentration at 10/1 in order to ensure that concentrations of complexes higher than the 1:1 would be negligible. (Maximum concentrations of Ln^{3+} and ligand were 0.40 and 0.04 M, respectively.) The pH of each solution was adjusted to the range 5.8 to 6.0 using a Chemtrix pH meter (type 40 AC) with accompanying combination glass electrode. The concentrations of the rare earth solutions were determined by titration with excess standardized EDTA which was back titrated in boric acid–NaOH buffered media at pH 8.5 with standardized Zn^{2+} solution and Eriochrome Black T as indicator (12).

Proton NMR spectra were recorded at 90 MHz with a Bruker WH-90 Fourier transform spectrometer at an operating temperature of $25 \pm 1^\circ\text{C}$. Induced shift values were measured relative to the shifts of diamagnetic La^{3+} solutions with similar Ln^{3+} concentrations, ligand concentrations, and pH values. Sodium 2,2-dimethyl-2-silapentane-5-sulfonate (DSS) was used as an internal reference.

The T_1 measurements were made with a 180° – τ – 90° inversion–recovery pulse sequence (13). Spherical microtubes containing approximately 25 μl were used in the determinations (Wilma Glass Company). In most cases the total concentration of La^{3+} and Gd^{3+} was held constant at 10^{-2} M, while the Gd^{3+} concentration was varied from 10^{-5} to 10^{-3} M. The ligand concentration was usually held constant at 0.04 M.

In the course of evaluating a suitable reference compound, we found that DSS coordinates to the Ln^{3+} ions. The variation of the observed $1/T_1$ with $[\text{Gd}^{3+}]$ depends on the particular proton, increasing in the order: $\text{Si}(\text{CH}_3)_3 < \gamma\text{-CH}_2 < \beta\text{-CH}_2 < \alpha\text{-CH}_2$. Similar variations for acetone and t-butanol were about half as large as that of the $-\text{Si}(\text{CH}_3)_3$ group of DSS. We also found that the α -, β -, and $\gamma\text{-CH}_2$ groups are shifted (≤ 100 Hz) but the chemical shift of the $-\text{Si}(\text{CH}_3)_3$ moiety remains unchanged when referenced against acetone in the presence of 0.4 M Dy^{3+} . Consequently, DSS proved suitable as a reference in the Ln^{3+} shift studies but less preferable in the T_1 studies. However, the use of DSS as a reference produced at most a 4% error in the T_1 ratios of the systems studied.

The computer search for a best-fit orientation of the principal magnetic axis and the Ln–O distance assumed free rotation of the carboxylate group and the methyl groups and systematically varied the Ln–O bond distance from 2.0 to 3.0 Å and the orientation of the principal symmetry axis from 0 to 90° in 5° increments.

¹ Reference to brand or firm name does not constitute endorsement by the U.S. Department of Agriculture over others of a similar nature not mentioned.

RESULTS AND DISCUSSION

Solvent Effects

Since the solvent system employed in these studies was aqueous d_6 -DMSO (to prevent precipitation), it was necessary to ascertain the effect of DMSO upon the lanthanide-ligand complex. Intramolecular shift ratios are expected to be sensitive to changes in coordination geometry or shift mechanism. Table 1 contains the ortho/meta and para/meta shift ratios of benzoate induced by Yb^{3+} at various percentages of DMSO. Although 100% DMSO changed the shift ratios significantly over those at 0% DMSO, concentrations of up to 30% DMSO (the maximum DMSO concentration employed) had negligible effect upon the shift ratios. Similar results were obtained for all other lanthanide ions employed.

TABLE 1
 Yb^{3+} -INDUCED SHIFT RATIOS OF BENZOATE
PROTONS AS A FUNCTION OF SOLVENT COMPOSITION

% DMSO ^a	ortho/meta	para/meta
0	3.10 ± 0.05	0.75 ± 0.02
5	3.11	0.75
15	3.16	0.75
20	3.14	0.75
30	3.18	0.72
100	3.62	0.64

^a Percentage by volume in DMSO- D_2O solvent.

Ln^{3+} -Induced Shifts

The lanthanide ion-induced shifts are generally attributed to a dipolar (pseudocontact) mechanism described by (14-17)

$$\frac{\Delta\nu}{\nu_0} = A\langle S_z \rangle + D \left(\frac{3 \cos^2 \theta - 1}{r^3} \right) + D' \left(\frac{\sin^2 \theta \cos 2\phi}{r^3} \right). \quad [1]$$

Here $\Delta\nu/\nu_0$ is the fractional shift at a nucleus located at a distance r from the center of magnetic anisotropy; A is the hyperfine coupling constant; $\langle S_z \rangle$ is the projection of the total spin magnetization on the magnetic field axis; θ is the angle between the vector r and the principal Z axis of the magnetic susceptibility; ϕ is the angle between the equatorial projection of r and the principal X axis; and D and D' are elements of the magnetic anisotropy.

If the anisotropic distribution of the paramagnetic center has axial symmetry, the third term vanishes and the equation reduces to

$$\Delta\nu/\nu_0 = A\langle S_z \rangle + DG, \quad [2]$$

where G is the geometric factor $(3 \cos^2 \theta - 1)/r^3$.

If data are available for a series of lanthanide ions, a graphical method is convenient for interpreting the results (16, 17). Equation [2] is rearranged to yield

$$(\Delta\nu/\nu_0)/\langle S_z \rangle = A + DG/\langle S_z \rangle. \quad [3]$$

Since values for $\langle S_z \rangle$ and D are obtainable from published calculations (18, 19), the induced shifts can be appropriately adjusted and plotted against the corresponding values of $D/\langle S_z \rangle$. If the assumption of axial symmetry holds and the geometry of the complex is constant across the lanthanide series, then the individual points should lie in a straight line. The results for the ortho proton of the *o*-toluate complexes are shown in Fig. 1.

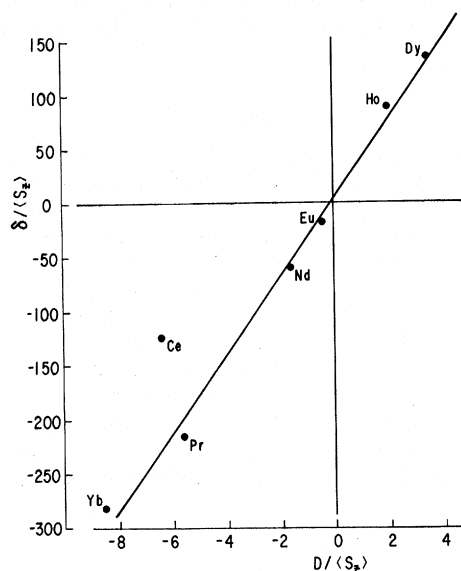


FIG. 1. Ln^{3+} -induced shifts of the ortho proton of the *o*-toluate complexes plotted according to Eq. [3]. Values for $\langle S_z \rangle$ and D were taken from Refs. (18) and (19), respectively.

With the exception of the Ce^{3+} result, the data fall very close to a straight line. The correlation coefficient for the remaining six points is 0.996. Results for the other proton resonances show good correlations as well, the correlation coefficient ranging upward from 0.97 with the Ce^{3+} data excluded. In all cases, the linear least-squares line runs nearly through the origin. For example, the Y intercept of the straight line in Fig. 1 is 4.6. Consequently, contact contributions to the induced proton shifts of the benzoate and toluate complexes appear to be negligible. The induced shifts seem to arise generally from a pseudocontact interaction which is primarily axially symmetric. Moreover, the fact that the linear relationship holds across the lanthanide series provides good evidence that the complex is isostructural for all ions.

This result is also reinforced by Table 2. Here, the proton shifts induced by the various ions relative to those of the Dy^{3+} complex measured under the same conditions are compared with the pseudocontact values based on an axially symmetric model (19). Good agreement of the experimental data with theory is noted for all ions except Ce^{3+} , which has shifts about one-half the predicted value, and Er^{3+} , which produces shifts

TABLE 2
COMPARISON OF THE SHIFTS INDUCED BY VARIOUS Ln^{3+} IONS WITH THOSE INDUCED BY Dy^{3+} FOR
o- AND *p*-TOLUATE^a

Ln^{3+}	H_{ortho}	H_{meta}	H_{para}	$\text{CH}_3_{\text{ortho}}$	$\text{CH}_3_{\text{para}}$	Theory ^b
Ce	-3.2	-3.5	-3.7	-3.5	-3.3	-6.3
Pr	-11.0	-12.3	-12.8	-12.5	-11.1	-11.0
Nd	-3.8	-3.8	-3.9	-3.9	-4.0	-4.2
Eu	5.1	6.0	4.2	6.6	4.6	4.0
Dy ^c	-100.0	-100.0	-100.0	-100.0	-100.0	-100.0
Ho	-46.6	-46.0	—	—	-48.3	-39.0
Er	11.8	12.9	—	—	9.9	33.0
Yb	18.9	18.6	17.7	17.6	16.4	22.0

^a Measured at 0.40 M Ln^{3+} concentration, 0.04 M ligand concentration, and a pH of 6.0.

^b From the theory of Bleaney *et al.* (19) for axial symmetry and constant structure.

^c The Dy^{3+} shifts are downfield and are of the magnitudes 42.9, 12.95, 10.53, 22.45, and 7.5 ppm, respectively.

only one-third the predicted magnitude.² Therefore, the results for Ce^{3+} are anomalous here as well as in the linear least-squares plots. On the other hand, the Er^{3+} result falls in line in Fig. 1 but not in Table 2 for reasons which are not as yet understood.

Another useful indicator of the nature of the induced shifts is the shift ratio. As can be seen from Eq. [2] for the axially symmetric case, if the contact term is negligible, then the induced shift is a function only of the appropriate geometric term and the constant, D , characteristic of the complexing ion. Consequently, for the ratio of the shifts of two magnetic nuclei in the same molecule, the D term cancels out and the ratio is dependent only on their respective geometries and is independent of the Ln^{3+} ion inducing the shifts. Therefore, the invariance of the shift ratios observed with a series of lanthanide ions is an excellent test for axial symmetry. In order to show axial symmetry by this test, however, the shift ratios should not vary more than a few percent, as pointed out recently by Sykes and co-workers (6, 7, 9).

TABLE 3
LANTHANIDE-INDUCED SHIFT RATIOS OF *o*-TOLUATE, *p*-TOLUATE, AND BENZOATE AT
pH 6.0

Ln^{3+}	$\text{H}_{\text{meta}}/\text{H}_{\text{ortho}}^a$	$\text{H}_{\text{para}}/\text{H}_{\text{ortho}}^b$	$\text{CH}_3_{\text{ortho}}/\text{H}_{\text{ortho}}$	$\text{CH}_3_{\text{para}}/\text{H}_{\text{ortho}}$
Ce	0.34	0.32	0.64	0.17
Pr	0.34	0.30	0.60	0.19
Nd	0.35	0.33	0.61	0.17
Eu	0.40	0.23	0.70	0.16
Dy	0.31	0.25	0.53	0.18
Ho	0.30	0.24	0.47	0.19
Er	0.33	0.23	0.45	0.16
Yb	0.31	0.23	0.50	0.16

^a This is an average for all three compounds.

^b This is an average for benzoate and *o*-toluate.

² The meta protons for the *o*-toluate complexes display different induced shifts for several of the ions. The pertinent values listed in the tables are the meta proton averages.

The shift ratios induced by various Ln^{3+} ions for *o*-toluate, *p*-toluate, and benzoate are given in Table 3. The values divide the table into three categories: Ce, Pr, and Nd, with very constant ratios having one set of values; Dy, Ho, Er, and Yb, with relatively constant ratios with another set of values; and Eu, whose ratios differ from both sets.

The results for Ce, Pr, and Nd are sufficiently close to satisfy the stringent test for axial symmetry. The ratios for Dy, Ho, Er, and Yb are also very close and indicate at most only small nonaxial contributions. The results for Eu suggest the presence of contact and/or nonaxial terms.

Clearly, these results are at odds with the linear least-squares plots. The shift ratio criterion appears to be a more demanding test of the nature of the induced shifts than the graphical interpretation. The ratios suggest a division of the rare earth ions into two major groups with different structural features. Such changes have been observed in similar rare earth systems and have been interpreted as arising from a change in the coordination (monodentate–bidentate) from the first half to the second half of the rare earth series (3, 20).

The linear least-squares plots appeared to show constant geometry across the entire series. However, on closer examination of the plots (for example, as in Fig. 1) it can be seen that Pr, Nd, and Eu consistently lie on one side of the straight line, while Dy, Ho, and Yb lie on the other side. If these are treated as separate cases, the least-squares lines from Fig. 1 are given by

$$\begin{aligned}\delta/\langle S_z \rangle &= 38.2 \times D/\langle S_z \rangle - 1.2 && \text{for Pr, Nd, Eu,} \\ \delta/\langle S_z \rangle &= 34.9 \times D/\langle S_z \rangle + 15.3 && \text{for Dy, Ho, Yb.}\end{aligned}$$

Similar results are obtained for the other proton positions. In all cases, the heavier elements show somewhat smaller values for the geometric factor and positive contact terms. For the lighter elements, the contact terms are very close to zero. Overall, the differences predicted for the geometric factors for the lighter and heavier members are small and could be accounted for as well by the presence of small nonaxial contributions.

An additional piece of information concerning the nature of the complexes comes from the nonequivalent induced shifts for the meta protons of the *o*-toluate complexes. The meta protons display differences in their induced shifts with Eu, Dy, Er, and Yb complexes, the magnitude of the differences ranging from 5 to 10% of the total induced shift. In those cases in which an assignment could be made, the meta proton adjacent to the methyl group showed the smaller induced shift.

However, two explanations seem plausible. If the metal ion binding in the latter half of the rare earth series were monodentate, the greater steric hindrance of the ortho methyl group would tend to cause preferential binding of the metal ion to the oxygen further removed from the methyl group, that is, on the side of the molecule containing the meta proton which has the greater induced shift. This would confirm the change in binding with the heavier Ln^{3+} ions. On the other hand, the nonequivalence could arise from different contact interactions at the two meta protons as mediated by the effect of the ortho methyl group adjacent to one of them.

In any event, there is sufficient evidence for axial symmetry and no contact contributions for the complexes of the lighter elements to justify comparing them with the axially symmetric bidentate model. The fitting process was carried out in a

computer program that systematically varied both the Ln–O bond distance and the orientation of the principal symmetry axis (0 to 90°) while including free rotation of the carboxylate group. The best agreement between calculated shift ratios and the averaged values for Ce³⁺, Pr³⁺, and Nd³⁺ was obtained by the 0° orientation of the principal symmetry axis with an Ln–O distance of 2.2 ± 0.1 Å. The agreement, as shown in Table 4, is very good.

TABLE 4
LANTHANIDE-INDUCED SHIFT RATIOS OF *o*-TOLUATE,
p-TOLUATE, AND BENZOATE AT pH 6.0

Ratio	Ce ³⁺ , Pr ³⁺ , Nd ³⁺ (average)	Computer best fit
H _{meta} /H _{ortho}	0.62	0.65
H _{para} /H _{ortho}	0.18	0.22
CH ₃ _{ortho} /H _{ortho}	0.34	0.37
CH ₃ _{para} /H _{ortho}	0.32	0.31

Spin–Lattice Relaxation

Data on the spin–lattice relaxation time (T_1) of a nucleus in a molecule coordinated to a paramagnetic metal ion also provide structural information on the complex. The quantity T_1 for a specific nucleus, I, is given by (21–23)

$$\begin{aligned} 1/T_{11} = & \frac{2}{15} \frac{\gamma_I^2 S(S+1) g^2 \beta^2}{r^6} \left(\frac{3\tau_c}{1 + \omega_I^2 \tau_c^2} + \frac{7\tau_c}{1 + \omega_s^2 \tau_c^2} \right) \\ & + \frac{2}{3} S(S+1) \left(\frac{A}{h/2\pi} \right)^2 \left(\frac{\tau_s}{1 + \omega_s^2 \tau_s^2} \right), \end{aligned} \quad [4]$$

where γ_I is the nuclear gyromagnetic ratio, S is the total unpaired electron spin on the metal ion, g is the g factor for the electrons, r is the distance between the paramagnetic metal ion and the nucleus undergoing relaxation, β is the Bohr magneton, τ_c and τ_s are the correlation times for dipolar relaxation and the electronic relaxation, respectively, ω_I and ω_s are the nuclear and electronic Larmor precessional frequencies, respectively, h is Planck's constant, and A is the electron–nuclear contact interaction coupling constant.

The parameter T_{11} is not directly measurable but is related to the measured value, T_{1m} , as indicated below (24).

$$\frac{1}{T_{1m}} = \frac{f}{T_{11} + \tau_m} + \frac{1-f}{T_{1u}} + \frac{1}{T_{1B}} \quad [5]$$

where T_{1u} is T_1 of the uncomplexed ligand, T_{1B} is the bulk relaxation time due to the presence of the metal ion in solution, τ_m is the lifetime of the bound state, and f is the fraction of bound ligand.

If the total Ln³⁺ concentration is held constant while the amount of paramagnetic ion is varied (with La³⁺ and Gd³⁺), then the fraction of ligand bound to Gd³⁺ is given by

$$f_{Gd} = \frac{[Gd]}{[Gd] + [La]} f_T = K[Gd], \quad [6]$$

where f_T is the total amount of ligand bound to both metals. Since f_T is constant and $[Gd] + [La]$ is held constant, the fraction of ligand bound is equal to a constant times the Gd^{3+} concentration. By substituting for f_{Gd} in Eq. [5], differentiating with respect to $[Gd]$, and rearranging, the following equation results.

$$d\left(\frac{1}{T_{1m}}\right)/d[Gd] - d\left(\frac{1}{T_{1B}}\right)/d[Gd] = K\left(\frac{1}{T_{1I} + \tau_m} - \frac{1}{T_{1u}}\right). \quad [7]$$

Since $1/(T_{1I} + \tau_m)$ ranges from 10^2 to 10^5 and $1/T_{1u}$ ranges from 10^{-1} to 4, the latter term can be ignored and the right-hand side of Eq. [7] reduces to the term $K[1/(T_{1I} + \tau_m)]$. The term $d(1/T_{1m})/d[Gd]$ is determined from the slope of a plot of $1/T_{1m}$ versus Gd^{3+} concentration at a constant total lanthanide concentration, and the term $d(1/T_{1B})/d[Gd]$ is determined from the slope of a similar plot for an inert reference compound.

Ratios of $1/(T_{1I} + \tau_m)$ for different protons can be obtained directly from the ratios of the appropriate quantities as described above. These are listed in the first column of Table 5.

TABLE 5
MEASURED AND PREDICTED $1/T_{1I}$ RATIOS FOR A BIDENTATE
CARBOXYLATE GROUP

Ratio	$1/(T_{1I} + \tau_m)$	$1/T_{1I}^a$	Predicted range ^b
H_{ortho}/H_{meta}^c	7.0 ± 0.6	11	12.3–8.67
$H_{ortho}/CH_3 para$	22.2 ± 1.5	37	45.4–27.9
$H_{meta}/CH_3 para$	3.2 ± 0.2	3.3	3.7–3.2
$H_{ortho}/CH_3 ortho$	1.81 ± 0.2	2.4	0.76–0.75

^a Corrected for a τ_m of 7.5×10^{-6} sec.

^b Predicted from bidentate binding of the carboxylate group with a Ln–O distance in the range 2.0 to 3.0 Å.

^c For the ortho proton, $1/(T_{1I} + \tau_m) = (9.14 \times 10^5/K) M^{-1} \text{ sec}^{-1}$, where K is the total fraction of bound ligand divided by the total metal concentration.

Contributions of τ_m to the observed relaxation times for complexes of this type are usually ignored since τ_m is on the order of 10^{-6} – 10^{-5} sec. However, the contribution in these systems can be evaluated readily from a knowledge of the equilibrium constants (approximately 50 L/M for the formation of the 1:1 ligand-to-metal complex). Under the conditions of ligand and metal ion concentrations used for these experiments, K in Eq. [6] takes the value 16.6 L/M. $T_{1I} + \tau_m$ can now be evaluated from the relaxation time data, the appropriate τ_m adjustment made (we used the value 7.5×10^{-6} sec), and the corrected $1/T_{1I}$ ratios determined. These are shown in the second column of Table 5.

The agreement between predicted and observed ratios for the *p*-toluate complexes is excellent. However, the observed ratio for the $H_{ortho}/CH_3 ortho$ for *o*-toluate is much higher than predicted. Moreover, taking the value of τ_m into account brings the first three ratios into the middle of the predicted range but makes the agreement for the

$H_{\text{ortho}}/CH_{3\text{ortho}}$ ratio even poorer. The ortho methyl group is expected to have a shorter T_1 than the ortho proton of *o*-toluate, since on the average the methyl protons are closer to the paramagnetic ion, but the reverse is actually found.

We also obtained Mn^{2+} relaxation data for *o*-toluate and found the $H_{\text{ortho}}/CH_{3\text{ortho}}$ $1/T_1$ ratio to be $\sim 1.3/1$, which confirmed the trend obtained with Gd^{3+} .

These findings at first suggest that a contact interaction may be responsible for the greater relaxation of the ortho proton since the magnitude of such an interaction would be greater for the ortho proton than for the ortho methyl group. However, in order that the contact term contribute significantly to the relaxation rate, the coupling constant required (see Eq. [2]) would be of the order of 10^7 Hz. (This estimate is based on a value for $1/T_{1i}$ for the ortho proton of $4 \times 10^4 \text{ sec}^{-1}$ and τ_s equal to 10^{-9} sec (22, 23).)

This is two orders of magnitude larger than that estimated for water protons from Gd^{3+} -induced proton shifts of H_2O (25). Moreover, a contact coupling constant of $\sim 10^7$ Hz would produce a 100- to 500-Hz shift in the ortho proton resonance position, whereas we observed a negligible shift (< 2 Hz). Therefore, a contact mechanism cannot be responsible for the greater relaxation rate of the ortho proton.

Monodentate binding of the gadolinium ion to the carboxylate group could explain the shorter than expected relaxation time for the ortho protons. In a monodentate system, the metal ion would probably preferentially bind the oxygen closer to the ortho protons as a result of steric hindrance, as mentioned previously. Such a difference could account for the shorter time since even a small decrease in the average distance between the ortho protons and the metal ion would have significant effects here because of the $1/r^6$ dependence of the relaxation times.

Another possible explanation may lie in the internal rotation of the ortho methyl group. If the methyl group rotation has a characteristic lifetime less than the correlation time characterizing the ortho proton relaxation, then the correlation times for dipolar relaxation would be different for the two groups. Using the experimental value for T_1 for the ortho proton and a value for r equal to 5.0 Å (Ln–O distance of 2.4 Å), the dipolar correlation time of the ortho proton calculated from Eq. [2] is 4×10^{-10} sec. This value is in agreement with a τ_c of 1.2×10^{-10} sec for Gd^{3+} –*N*-acetyl-L-3-nitrotyrosine ethyl ester (6) and is of the order expected for molecular tumbling for complexes of this size.

The characteristic lifetime (τ) for rotation about a chemical bond is given by (26)

$$\ln(1/2\tau) = \ln A - E_a/(RT), \quad [8]$$

where A is a frequency factor for torsional reorientation and E_a is the barrier to rotation. Using a value of A appropriate to small molecules (10^{13} sec^{-1}) (27, 28) and an energy barrier to methyl group rotation of 4 kcal/mole (29), the lifetime of a given state is estimated to be 2.6×10^{-11} sec, a value much shorter than the molecular tumbling rate. Consequently, the correlation time for the ortho methyl group may be dominated by the rate of internal rotation, which may lead to less effective relaxation by the paramagnetic center. Although the values for the torsional reorientation frequency and the energy barrier given above are estimates only, the above calculation serves to demonstrate the possibility of shortening the effective correlation time by torsional motion and thereby reducing the relaxation. The correlation time of the ortho methyl protons relative to the ortho proton would have to be decreased only by a factor of 3 in order to account for the observed discrepancy.

CONCLUSION

The Ln^{3+} -induced shifts and relaxation times observed in the conformationally rigid systems of *o*-toluate, *p*-toluate, and benzoate complexes seem to offer a number of contradictory interpretations. Nevertheless, several salient features emerge from the various treatments of the data.

First, the induced shifts generally are consistent with an axially symmetric model with negligible contact interactions. This is borne out by the linear least-squares plots, the correlations with the predictions of the axially symmetric model, and the constancy of the shift ratios. Not all ions are consistent throughout and in some instances correlations are probably coincidental through the canceling of opposing contributions.

Second, there is a strong suspicion that the binding is not identical throughout the entire Ln^{3+} series. The changes between the lighter and heavier members, however, must be rather subtle since the differences which arise are relatively small and do not appear to require the drastic change in binding from bidentate to monodentate, as evidenced in some other systems. The differences are sufficiently minor, in fact, to be explainable by small nonaxial or contact contributions.

Third, the relaxation times offer important additional information about these systems and confirm the bidentate model for most of the proton relaxation data. The ratio of the relaxation time of the ortho proton to the ortho methyl protons is an exception. A deviation from the bidentate model is the most facile explanation for this anomaly but changes in the correlation time of the methyl protons due to the rapid internal rotation also offer a possible solution.

The result that the induced shifts appear to be pseudocontact in origin with axial or near axial symmetry is encouraging to attempts to obtain structural information from the induced shifts of the Ln^{3+} complexes of more flexible molecules. Since the geometry of the complex is undoubtedly dominated by the effect of the carboxylate group, these results can be extrapolated with some confidence to complexes of relatively complicated molecules undergoing internal rotation. Furthermore, these results confirm the validity of a number of previous studies in which the presence of axial symmetry had only been assumed.

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